AIFA notice

(update of the AIFA notice published on 12 March 2020)

Clinical trials' management in Italy during the COVID-19 (*coronavirus disease 19*) emergency (Version 2 of 7 April 2020)

Following the number of requests received by the Clinical Trial Office/Pre-Authorization Area and by the GCP Inspections Office from the various stakeholders, the Italian Medicines Agency provides indications regarding the management of clinical trials and substantial amendments in Italy after the exceptional restrictive measures introduced by the Italian Government in order to fight the COVID-19 (*coronavirus disease 19*) pandemic, valid until further notice and strictly linked to the state of emergency approved by the Council of Ministers on 31 January 2020.

Clinical trials must be conducted according to common sense principles, with the highest protection of trial participants and maintaining adequate supervision by the Principal Investigators (PIs). To this end, please consult the *Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic* published on the European Commission website, EudraLex Volume 10 Clinical trials (https://ec.europa.eu/health/documents/eudralex/vol-10_en).

Submission of clinical trials and substantial amendments

Following what already set down in the previous notice, AIFA clarifies that, also in this period of emergency due to the COVID-19 (*coronavirus disease 19*), the submission of authorization requests for clinical trials and substantial amendments must be done through the OsSC, according to current rules. Anyway, considering that many pharmaceutical companies, no-profit Sponsors and CROs have applied smart-working in order to continue their activities related to clinical trials, AIFA will validate/evaluate requests submitted by the OsSC even if relevant paper documentation and CD-rom have not yet arrived (however, they will have to be sent as soon as possible). It is anyway recommended, if applicable, to apply the stamp duty on the cover letter by virtual payment (except in the cases provided for in art. 17 of the Legislative Decree no. 460/1997 and in art. 82, par. 5 of the Legislative Decree no. 117/2017). In case this is not possible, the paper stamp duty will have to be applied on the cover letter and the letter will have to be scanned and uploaded to the OsSC. For more details, please refer to the notice "Applications filed electronically to the Italian Medicines Agency: stamp duty method of payment" published on the AIFA website on 26 March 2020 (https://www.aifa.gov.it/-/istanze-presentate-all-agenzia-italiana-del-farmaco-per-via-telematica-modalita-di-assolvimento-dell-imposta-di-bollo).

In case the submission via OsSC is not possible due to system's malfunctions or technical obstacles, it will be necessary to adopt the temporary paper transmission way. Transmission by e-mail will not be accepted. Exception is made only for the submission of clinical trials for the treatment of COVID-19 (*coronavirus disease 19*): authorization requests are allowed to be submitted by e-mail to apa@pec.aifa.gov.it (and to sperimentazione.clinica@aifa.gov.it in Cc), if the submission via OsSC is not possible. However, any responses to integration requests in the validation phase or to grounds

for non-acceptance in the evaluaton phase can be sent by e-mail. Such documentation will be evaluated without waiting for the paper documents and the final provision will be issued, being understood that paper documentation must be sent as soon as possible.

Submission of clinical trials and substantial amendments of studies for the treatment of COVID-19

As far as submission of clinical trials for the treatment of COVID-19 (*coronavirus disease 19*) in general, it is necessary to comply with provisions set down by the circular published on the AIFA website (https://www.aifa.gov.it/-/circolare-sulle-procedure-semplificate-per-gli-studi-e-gli-usi-compassionevoli-per-l-emergenza-da-covid-19), as required by art. 17 of the Law Decree of 17 March 2020, no. 18 containing "Measures to strengthen the National Health Service and economic support for families, workers and businesses connected to the epidemiological emergency from COVID-19", called "Cura Italia".

According to the afore-mentioned Law Decree, clinical trial protocols are preliminarily evaluated by the AIFA Technical Scientific Committee (CTS) and subsequently approved, after evaluation by the AIFA Competent Authority (Clinical Trial Office) and by the Ethics Committee of the National Institute for Infectious Diseases Lazzaro Spallanzani in Rome, as single national Ethics Committee for the evaluation of clinical trials of medicinal products for human use and medical devices for patients affected by COVID-19 which expresses the national opinion, also on the basis of the evaluation of the AIFA's CTS.

Only for clinical trials for the treatment of COVID-19 (*coronavirus disease 19*) in general, in case the submission via OsSC is not possible, the submission of authorization's requests can be done adopting the temporary paper transmission or through the mailbox apa@pec.aifa.gov.it, and supporting documentation can be sent preferably via Eudralink or similar ways (suitable for the secure sending of confidential documentation) within the same e-mail.

Please note that, according to art. 17, paragraph 3 of the Law Decree of 17 March 2020, no. 18, since the Ethics Committee of the National Institute for Infectious Diseases Lazzaro Spallanzani in Rome have to issue the national single opinion, it must be identified as the coordinating Ethics Committee and, therefore, the National Institute for Infectious Diseases Lazzaro Spallanzani in Rome must be identified as the coordinating site. This does not necessarily mean that PIs of the Institute must be involved (only "Ethics Committee" can be indicated instead of name and surname of the PI).

Please also note that, according to paragraph 2, second sentence of art. 17 of the afore-mentioned Law Decree, AIFA will take care of sending the protocol and synopsis of the study in object to the Technical Scientific Committee (CTS) for its preliminary assessment.

We also inform you that an accelerated timing is foreseen for the evaluation of COVID-19 studies.

Finally, it is recommended to include the wording "COVID-19" in the clinical trials title for their easier identification, as well as in the subject field and text of the e-mail in the event that this transmission way is used.

For the supporting documentation to the authorization's request of clinical trials for the treatment of COVID-19 (*coronavirus disease 19*) in general, please refer to the document list provided in the OsSC (in case of submission through the temporary paper transmission or through the apa@pec.aifa.gov.it mailbox, in addition to the documentation listed below, you must also submit the authorization request form or Appendix 5 and the XML file):

Core Documentation

- General information (if applicable, delegation letter from the Sponsor to the Applicant)
- Protocol information (protocol*, Italian synopsis*, any peer review, R/B assessment, special populations inclusion assessment, ethical assessment by the coordinating investigator)
- IMP information (IB*, or SmPC*)

Documentation for Competent Authority and national Ethics Committee

- General information (cover letter to AIFA*, Competent Authorities list of other countries involved and their decisions, summary of any scientific advices, copy of EMA decision and opinion on a PIP, receipt of the fee payment* - N.B.: it is mandatory in the OsSC, but it can be replaced by an explanatory Word document if not applicable)
- IMP information (IMPD* or simplified IMPD* or SmPC*, GMP authorization for manufacturing and import* for sites involved in the manufacturing/analysis/packaging, including labelling/import if applicable/release – N.B. it is mandatory in the OsSC, but it can be replaced by an explanatory Word document if not applicable, QP declaration of compliance to EU GMP for extra-EU sites, IMP certificate of analysis if not already included in the IMPD, authorization statuses applicable to particular IMPs like radiopharmaceuticals, narcotics and GMO contents, TSE compliance certificates, IMP label in Italian*) (for details, see the *Guide to the CTA section D compilation*: https://www.aifa.gov.it/documents/20142/871583/Guida_alla_compilazione_Appendice_5_Sezione_D_25.01.2019.pdf
- NIMPs information

Site-specific Documentation (only for the national Ethics Committee)

- General information (cover letter to the Ethics Committee*, receipt of the fee payment* - N.B.: it is mandatory in the OsSC, but it can be replaced by an explanatory Word document if not applicable)
- Subjects information (informed consent form*, package leaflet, recruitment procedures, material for participants, letter for the treating physician)
- IMP information (clinical trials/uses and B/R assessment, if not described in the IB)
- Structures, staff and financial arrangements (principal investigator CV* N.B.: it is mandatory in the OsSC, but it can be replaced by an explanatory Word document if not applicable, proposed contract between Sponsor and investigational site, insurance certificate*, auxiliary staff, any compensation for loss of earnings/reimbursement of participants expenses)

  where * indicates a mandatory document

Please note that to the CTS, for the preliminary assessment, only the protocol and synopsis will be forwarded by the Clinical Trial Office/Pre-Authorization Area, while the IB only on request.

The sites that will be involved in the study, in addition to the National Institute for Infectious Diseases Lazzaro Spallanzani in Rome, will be included as collaborating sites in section G.2 of the Clinical Trial Application (CTA or Appendix 5) and the related Ethics Committees, although not formally called to issue their opinion, must accept the single opinion of the national Ethics Committee by filling in the Appendix 8 if the CTA has been submitted via OsSC since the beginning.

For COVID-19 studies in OsSC, any substantial amendments to be evaluated must be submitted to AIFA, to the national Ethics Committee for its opinion and to the other Ethics Committees that will accept the opinion as indicated above.

In particular, as regards the possible addition of sites to already approved clinical trials, since the Ministerial Decree of 21 December 2007 does not envisage the coordinating Ethics Committee's opinion but only that of the Ethics Committee of the new site to be involved, only for COVID-19 studies it is possible to proceed via OsSC by submitting a "pre-existent" substantial amendment adding the site, so as not to have to obtain the opinion of the Ethics Committee relating to the new site. In this case, the date to be indicated as the date of the concerned Ethics Committee's opinion will be the one in which it was decided to include the new site.

For COVID-19 studies not in the OsSC, substantial amendments to be evaluated must be submitted to AIFA (apa@pec.aifa.gov.it) and to the national Ethics Committee (comitatoetico@inmi.it).

For multinational studies, please consider the possibility to submit them as a Voluntary Harmonisation Procedure (VHP) and to contact EMA for any Scientific Advice procedure, both for an accelerated assessment, in accordance with the provisions of the *Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic*.

Also perspective pharmacological observational studies must be submitted to AIFA and to the National Institute for Infectious Diseases Lazzaro Spallanzani Ethics Committee in Rome.

Pharmacological observational study protocols will have to be sent at the same time to AIFA through the mailbox apa@pec.aifa.gov.it (sperimentazione.clinica@aifa.gov.it and info_rso@aifa.gov.it in Cc) and to the national Ethics Committee (comitatoetico@inmi.it). They will only be notified to any other Ethics Committee involved.

Ethics Committees evaluations of clinical trials/substantial amendments

Without prejudice to the current legislation and internal procedures of each single Ethics Committee, their meetings may also be held by web-conferences or other telematic ways, with a frequency appropriate to manage urgencies due to the current emergency.

Methods of communicating measures that cannot be postponed modifying the execution or management of clinical trials in order to comply with the measures adopted due to COVID-19

In the event that, to limit the risk of contagion from coronavirus, measures that cannot be postponed modifying the execution or management of clinical trials (including temporary changes to the protocol) in order to comply with the measures adopted due to COVID-19 are implemented, a notified substantial amendment must be submitted only to the Ethics Committees of the sites involved (in which patients concerned are followed), for ensuring accurate tracking of all deviations, but also to facilitate the rapid implementation of the measures avoiding further burdens to the structures concerned.

The notification as a substantial amendment for immediate implementation is also applicable to all the specific cases described later in this notice.

Whenever possibile, the substantial amendment must be notified via OsSC; otherwise, Appendix 9 must be produced and used for the temporary paper transmission way. In case of paper procedures, sending by e-mail (only to the concerned Ethics Committees) the notified substantial amendment is considered acceptable.

The amendment is necessary both to communicate that emergency measures are put in place and to communicate their end.

In both cases, the amendment must be notified and not submitted for evaluation. To this end, it is suggested to fill in the Appendix 9 by selecting Yes in the "D.2.2.3 Other" field and to fill in the "D.2.2.3.1 If other, specify" field. It should not be indicated that this is an urgent safety measure, but a notified amendment due to the COVID-19 emergency.

In the event that the Sponsor temporarily halts enrollment and/or treatment in a clinical trial, to comply with the measures in place due to COVID-19, it will be necessary to notify a substantial amendment to the Ethics Committees of the sites involved (regardless they have initiated the trial or not) both when the measure is introduced and when it is canceled.

Also in this case, it is suggested to fill in the Appendix 9 by selecting Yes in the "D.2.2.3 Other" field and to fill in the "D.2.2.3.1 If other, specify" field. This is because if the field "D.2.3.2 The amendment communicates a temporary halt of the trial" is selected in OsSC, the substantial amendment for the trial restart would be automatically submitted for evaluation.

For more details on how to communicate to the Competent Authority and to the Ethics Committees the actions taken/to be undertaken to protect participants in clinical trials, please refer to point 6. of the *Guidance on the Management of Clinical Trials during the COVID-19 (Coronavirus) pandemic*.

Management of clinical trial activities outside investigational sites

Investigators and Sponsors are invited to consider the opportunity to limit visits to those strictly necessary, canceling unnecessary ones and, where possible, also providing for the extension of the duration of the trial.

In this regard, taking into account provisions set down by DPCMs (Decrees of the Italian President of the Council of Ministers) concerning the urgent measures for the containment and management

of the epidemiological emergency from COVID-19 and by specific Ordinances issued by Regions, Sponsors/CROs are invited to draw up a risk assessment plan and implement a risk-proportionate action plan, for the maximum protection of trial subjects, in view of the urgent need to minimize contacts between patients and investigational staff, and not to overload healthcare facilities. Sponsors are also invited to inform experimental sites and to agree with them in time all the alternative measures, related to the contingent situation, adopted for the management of the trials' subjects.

Provided they are compatible with the feasibility at the subject's home, the carrying out of procedures directly at the patient's home, carried out by the experimental site staff or by third parties, may be considered. Such home health care activities may include both clinical procedures that cannot be carried out otherwise (e.g. collection of adverse events, vital signs, etc.), and the administration of non-self-administering therapies (e.g. infusions).

In reiterating that these measures must be understood as extraordinary and limited to the strict coronavirus emergency period, in derogation from FAQ 11 of the EMA document "*Q&A: Good clinical practice (GCP)*" - *GCP Matters* (https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice/qa-good-clinical-practice-gcp), the Sponsor/CRO is allowed to directly enter into contracts with these agencies/third party specialized companies. All other indications of the afore-mentioned FAQ remain applicable, and compliance with the rules on the protection of personal data, such as, for example:

- the need for maintaining the PI oversight
- efficient communication ways are established between the staff in charge and the PI
- that the staff in charge is properly trained and the related duties and responsibilities are indicated in the contract and/or delegation log
- that the confidentiality of sensitive personal data is guaranteed
- that the relations between these third parties and the investigational sites are governed pursuant to art. 28 of the General Data Protection Regulation 2016/679, through a contract or other legal act for the designation of data controller.

The Sponsor must ensure that the insurance stipulated for the clinical trial also covers the changes implemented for the coronavirus emergency.

Please note that, if the experimental sites (data controllers) entrust part of the activities aimed at ensuring treatment continuity to third parties (also through collaboration with the Sponsors), the relations between these third parties and the experimental sites must be governed pursuant to art. 28 of the General Data Protection Regulation 2016/679, through a contract or other legal act for the designation of a responsible for the personal data processing.

Investigational medicinal product (IMP) management

If possible, when the patient goes to the study site for a visit, it may be useful to provide an amount of medicinal product covering a longer period of time than is normally estimated; also, it should have an expiration date going beyond the scheduled treatment period to avoid erroneous intakes of expired IMP by the subject.

Moreover, if the subject can hardly reach the clinical site and to limit movements, the IMP can be delivered to a family member or other person (a caregiver, for example), who must have a delegation letter by the subject himself, as established by the law in such cases.

The evaluation of the period to be covered by larger amounts of IMP is carried out by the investigator, who must maintain constant control over the correct intake by the subject, in accordance with the clinical protocol. In this case, in fact, the supply of additional IMP corresponds in all and for all to a prescription by the investigator, with all the ethical, clinical and legal responsibilities connected to it.

Please note that, according to current legislation (art. 7 of the Ministerial Decree of 21 December 2007), the investigational medicinal products required for the trial must be sent by the Sponsor/CRO to the pharmacy of the health facility where the trial is held, which is in charge for their registration, appropriate storage and delivery to the investigator. Therefore, considering the COVID-19 serious emergency, even if the priority way remains the delivery to the hospital pharmacy, direct deliveries from the hospital pharmacy to the trial participants also through dedicated couriers can be arranged, upon indications of both the hospital pharmacy Director and the Principal Investigator (PI). The hospital pharmacy remains responsible for the process supervision; the pharmacy and the PI must be constantly informed on the delivery, according to procedures established for the correct conduction of the trial and by the risk plan mentioned in the introduction, that must take into account the IMP typology, administraton methods, conservation and transport.

In case the Sponsor/CRO has already identified or has an authorized warehouse, where the IMP is stored, given the highly restrictive provisions adopted at national level for the COVID-19 emergency aimed at reducing as much as possible additional travel and passage, source of further risk, direct delivery by the warehouse to the trial participant could be considered only for the period limited to the afore-mentioned emergency. If this way is chosen, procedures for maintaining all guarantees of control and traceability of delivery are to be identified, including shipping conditions and agreements in this regard with the experimental sites. It is moreover necessary to consider solutions such as the use of a dedicated courier, which operates according to procedures for the direct delivery of the experimental medicinal products to the participating subjects and which also implements all the measures aimed at guaranteeing the confidentiality of the subject information, such as the instructions pursuant to art. 29 of the GDPR, which the data controller is required to provide to anyone acting under his authority, or, if applicable, the designation of data controller pursuant to art. 28 of the GDPR.

GCP guidelines (§§ 5.14.4, 8.2.15 and 8.3.8) require that the Sponsor/CRO keep the IMP delivery documentation but these points clearly refer only to the shipment from the Sponsor/CRO to the investigational sites' hospital pharmacies. Since this is an extraordinary procedure, this does not apply to the direct delivery to the subjects' home and therefore the relative documentation must be kept directly at the experimental site for ensuring data confidentiality.

Suitable remote communication mechanisms with interested parties must be guaranteed in order to allow the exchange of all information that will no longer be provided in person. Depending on the cases, where deemed necessary, telephone and/or video-calls can be used to facilitate the information of the subject or provide detailed instructions. It is recommended to keep a recorded track of the communications, of any kind, occurring during this emergency situation.

All this without prejudice, if possibile, to conditions set out in FAQ 10 of the EMA Document "Q&A: Good clinicalpractice (GCP)" – GCP Matters (https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice/qa-good-clinical-practice-gcp).

If the CRA of the study is not able to carry out the control on the final accounting of the investigational medicinal product for the purpose of reconciliation, and this operation is considered as impossible to be postponed, it can be carried out by a pharmacist of the hospital pharmacy or by the study coordinator/data manager, subjects responsible for the personal data processing, pursuant to art. 2-quaterdecies of the Personal Data Protection, Legislative Decree of 30 June 2003, no. 196, appropriately trained. The IMP can be returned to the Sponsor/CRO directly by the hospital pharmacy.

Always for limiting travel and contacts as much as possible, it is considered acceptable, for those IMPs close to the expiry date, to adopt the solution of keeping, until the end of the emergency, the IMP at the hospital pharmacy, in areas specifically identified and segregated, putting in place the appropriate precautions, foreseen by a specific procedure, aimed at avoiding the erroneous use of expired or deteriorated IMP.

Clinical tests

With regard to the conduct of clinical and/or medical tests (e.g. CAT, MRI, X-ray) essential for the participants safety, being aware of the need they must be performed in laboratories near to the patient's home, public facilities should preferably be chosen; if private, they must be recognized as suitable for conducting clinical trials pursuant to the Ministerial Decree of 19 March 1998 or self-certified private laboratories pursuant to AIFA Determination 809/2015. The use of private facilities not in possession of such recognition of suitability or not self-certified, must be carefully evaluated and implemented only if it represents the unique possibility to protect the subjects safety; the subsequent use of the data produced by these facilities, if connected with the trial endpoints, should be explained and discussed in the study report.

It should be noted, as mentioned above, that, even in this case, the data controller (investigational site) is required to regulate relations with the afore-mentioned facilities pursuant to art. 28 of the GDPR, if they act in the name and on behalf of the data controller, or if they must be considered as independent data controllers, pursuant to art. 24 of the afore-mentioned Regulation.

Closing of sites

If a site is "closed" to the public for COVID-19 containment measures, it should be carefully assessed if the clinical trial staff is able to ensure the continuity of the trial itself. In case the trial staff is unable to follow the patients enrolled in the trial, the study should be temporarily halted or, where possible, enrolled patients should be transferred to the closest active trial site. Obviously, information exchange between the PIs of the two sites must be guaranteed, as well as the transmission of clinical documentation and other trial material (e.g. IMPs) between sites. In such cases, the complete transfer of the trial to another site involves the transfer of responsibility to the other PI of the new

site. In the case, instead, of a temporary transfer not of all the trial but of single procedures (for example visits) related to the study, the initial PI remains responsible for the trial.

Contracts between Sponsor/CRO and health facilities involved must be updated according to new agreements.

A site not authorized to participate in the specific clinical trial is not considered as suitable as back-up, since it is not active, it does not know the trial and could not ensure a proper clinical management of the patient.

Clinical trial monitoring

By analogy with what previously stated, Sponsors are invited to draw up a risk assessment plan and implement an action plan taking into account the need to reduce unnecessary contacts in this period of COVID-19 epidemiological emergency. First of all, it should be assessed whether on-site monitoring visits can be replaced by the introduction and/or an enhanced centralised monitoring or whether such local visits can be postponed.

Exceptional and alternative means such as telephone calls or, even better, video-calls with the trial site staff are accepted for the purpose of Source Data Verification (SDV).

If, in accordance with the Sponsor's risk assessment, the SDV cannot be postponed and, where appropriately justified by the intent to protect the rights and well-being of the participants under trial (GCP-ICH § 5.18.1 (a)), other remote monitoring methods (for example, temporary access to the data contained in the electronic medical records of the healthcare facility relevant for the purposes of the trial), can be considered; anyway, they must be clearly described in a procedure that must be agreed with all the subjects involved (e.g. the CRO) and having heard their respective Data Protection Officers (DPO), in accordance with the provisions of art. 37 and following of EU Regulation 2016/679.

Solutions that involve a burden of work for the investigational site staff are not acceptable (e.g. the provision of a large amount of redacted pdfs files).

Alternative methods can be implemented only if they can ensure that access will only be made to the documentation of the participants included in the trials, limited to the period of involvement in the trial and for the period of time in which the emergency conditions persist.

If suitable guarantees to protect the fundamental rights and freedoms of the interested parties exist, in fact, temporary and alternative monitoring methods can be put in place in consideration of the urgency or the undeferrable need for supervision by the Sponsor/CRO, according to ways established by the data controller and consistent with the security measures adopted by the controller himself that take into account the highest level of risk associated with this way.

When the situation is normalized, it is essential that robust follow-up measures are planned by the Sponsor/CRO to assess and eventually fill in the gaps due to the reduced frequency of on-site monitoring or the application of alternative measures.

Possibility of exceptional expenses reimbursement

Given that from the application of the emergency measures for COVID-19 there must be no additional cost for public finances or for individuals, taking into account this exceptional situation, if, in order to implement urgent measures for the protection of participants involved in a clinical trial, expenses may be borne initially by the participants, similarly to what is already allowed in extraordinary cases (e.g. trials on rare diseases), and the Sponsor/CRO is allowed to reimburse such expenses to the participants. In order to avoid direct contacts between subjects and Sponsor/CRO, the favourite way would be the shipment of the receipts or the delivery by the subject (when possible) to the experimental site, which will invoice this amount to the Sponsor/CRO and reimburse expenses, through its administration. The costs incurred must be adequately documented and the receipts issued by external facilities must clearly indicate the protocol code or the EudraCT number of the study.

Alternative procedures to obtain the Informed Consent

Given the current emergency situation, the inclusion and enrollment of new participants in clinical trials should be avoided as much as possible, except for those cases whose participation in the study is of fundamental necessity, such as in the absence of a valid therapeutic alternative, or of course, in cases of enrollment in studies where COVID-19 drugs are tested. In case it is necessary to obtain an informed consent (initiation of new studies or amendment to the informed consent for ongoing studies or for the implementation of emergency measures referred to in this notice or simply to avoid exchanges of paper material, which can be a possible source of contagion), where not possible in the usual way, alternative procedures for obtaining it must be considered. The implementation of such alternative procedures (telephone calls, followed by e-mail confirmation or validated electronic systems) does not exempt from obtaining written consent as soon as possible, on the first occasion in which the participant goes to the site.

The opportunity to acquire consent from the participants must always be privileged over other solutions, even in cases of subjects who are in physical isolation, for which cameras or photographs of the documentation can be taken through transparent isolation barriers.

In the case of a temporary oral consent, the presence of an impartial witness who certifies that the consent has successfully been given, by dating and signing the informed consent document, is required. The investigator is responsible for certifying how the impartial witness was selected.

In any case, rules on the personal data processing remain unchanged, with particular reference to the acquisition of the consent to the personal data processing itself carried out in the context of the clinical trial. According to the accountability principle, the data controllers are required to identify suitable measures and prove the successful acquisition of a valid consent to the personal data processing, for example through the voice recording of the consent given by phone or the e-mail keeping.

Compliance with the personal data protection rules

Without prejudice to the preliminary indications provided above also in relation to some fulfilments related to the personal data protection regulation, it is understood that it is up to each individual data controller to identify, if necessary, the technical and organizational measures necessary to ensure that these alternative methods for the clinical trials management comply with the personal data protection regulation set out in EU Regulation 2016/679, with the Personal Data Protection Code, with the deontological Rules for processing data for statistical or scientific research purposes published pursuant to art. 20, paragraph 4, of Legislative Decree 10 August 2018, no. 101 - 19 December 2018, attachment A5 to the Code, and to the Prescriptions relating to the personal data processing carried out for scientific research purposes, attachment no. 5 to the Measure containing the provisions relating to the processing of particular categories of data, pursuant to art. 21, paragraph 1 of Legislative Decree 10 August 2018, no. 101, dated 5 June 2019. In applying the COVID-19 emergency measures, in fact, the principles applicable to the personal data processing enshrined in EU Regulation 2016/679 must be respected, with particular reference to the principles of minimization, integrity and confidentiality of data (art. 5, paragraph 1, letters c) and f)), according to the solutions deemed, from time to time, more appropriate and suitable for the specific case. To this end, please note that each data controller can take advantage of the advice and support of the data protection officer, designated pursuant to art. 37 of the GDPR.

General considerations

The measures contained in this notice are of an exceptional nature and represent a derogation from the applicable rules and practices, therefore a CRO cannot proceed to apply these exceptional measures without informing the Sponsor, who, in accordance with the GCP, remains the final person responsible for the trial.